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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,453	04/16/2001	Dan M. Granoff	CHIR-0283	1041

7590 04/20/2009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
04/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/701,453	GRANOFF ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-22,24-28 and 30* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☒ Claim(s) *26,27 and 30* is/are allowed.

6)☒ Claim(s) *17-19,21,22,24 and 25* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed 01/23/09 has been entered.

Status of Claims

2) No claims have been amended.

Claims 17-22 and 24-30 are pending.

Claims 17-22, 24-28 and 30 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection to Specification

5) The specification is objected to for the following reason:

37 CFR 1.75(d)(1) provides, in part, that 'the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description.' The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR .75(d)(1) and MPEP § 608.01(o). The limitation 'a carrier **comprising** polyglycolic acid**s** or polyglycolic acid**s**' [Emphasis added] in claims 17 and 26 lacks clear support or antecedent basis in the specification.

Interpretation of Claims 24 and 28

6) Applicants state that they were mistaken in their interpretation of dependent claim 24. Applicants submit that claim 24 'claims a carrier comprising polylactic acids or polyglycolic acids'

as an alternative to CRM197, since 'independent claim 17 only claims a carrier'. Applicants state that the claimed invention in claim 24 is an immunogenic composition comprising MenC-capsular polysaccharide conjugated to polylactic acids or polyglycolic acids, MenB OMV, and MF59. See page 6 of Applicants' response filed 01/23/09.

However, claim 24 does not 'claim' a carrier comprising polylactic acids or polyglycolic acids', but recites one. This is also true with claim 28. The independent claim 17 does not 'claim' only a carrier, but claims an immunogenic composition wherein a first antigen as recited is conjugated to a carrier. Claims 24 and 28 recite that the composition comprises 'a carrier'. The limitation 'a carrier' is not the same as the limitation 'said carrier' with regard to the scope. Therefore, 'a carrier comprising polylactic acids or polyglycolic acids' in the composition of claims 24 and 28 is not the carrier recited in the base claims wherein a capsular oligosaccharide from NmC is *required* to be conjugated to. Therefore, 'a carrier comprising polylactic acids or polyglycolic acids' in the dependent claims 24 and 28 is interpreted as an additional carrier that is not required to be conjugated to a capsular oligosaccharide from NmC.

Rejection(s) Withdrawn

7) The rejection of claims 17-19, 21, 22 and 25 made in paragraph 8 of the Office Action mailed 10/26/07 and maintained in paragraph 5 of the Office Action mailed 07/23/08 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) in view of Seid Jr. *et al.* (US 7,118,757, already of record) ('757) and O'Hagan (*J. Pharm. Pharmaco.* 50: 1-10, January 1998, already of record), is withdrawn in light of the new rejection set forth below. Applicants' arguments have been considered, but are moot in light of the art rejection set forth below.

8) The rejection of claim 24 made in paragraph 9 of the Office Action mailed 10/26/07 and maintained in paragraph 6 of the Office Action mailed 07/23/08 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) as modified by Seid Jr. *et al.* (US 7,118,757, already of record) ('757) and O'Hagan (*J. Pharm. Pharmaco.* 50: 1-10, January 1998, already of record) as applied to claim 17, and further in view of Seid (US 6,638,513, already of record) ('513), is withdrawn in light of the new rejection set forth below. Applicants' arguments have been considered, but are moot in light of the art rejection set forth below.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

9) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10) Claims 24 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The dependent claims 24 and 28 include the limitation: wherein said composition comprises 'a carrier **comprising** polyglycolic acids or polyglycolic acids' [Emphasis added], which is not required to be 'said carrier' recited in the base claims 17 and 26 respectively and therefore is not conjugated to the first antigen. This means that polylactic acids or polyglycolic acids are contained within a generic carrier, which encompasses organic carrier, inorganic carrier, cellular carrier, bacterial carrier, polymeric carrier etc. However, there is no descriptive support for such a limitation in the as-filed specification. For example, the first full paragraph on page 4 of the specification requires that the first carrier is conjugated to the NmC oligosaccharide. The second full paragraph on page 4 of the specification is supportive of the first carrier in the immunogenic composition being 'a polylactic acid' or 'a polyglycolic acid', but does not support 'a carrier **comprising** polyglycolic acids or polyglycolic acids'. Lines 16 and 17 on page 4 of the specification describe that the immunogenic composition comprises a second carrier that is alum or MF59, and therefore the second carrier being polylactic acid or polyglycolic acid is not supported. There is no support for an immunogenic composition comprising a conjugate or non-conjugated third carrier, third carrier being a carrier **comprising** therein polyglycolic acids or polyglycolic acids. Therefore, the above-identified limitation in the claim(s) is considered to be new matter. New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed by pointing to specific lines and pages, for the new limitations, or alternatively, remove the

new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 103

11) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

12) Claims 17-19, 22 and 25 are rejected 35 U.S.C § 103(a) as being unpatentable over Granoff *et al.* (*Infect. Immun.* 65: 1710-1715, May 1997, of record) (Granoff *et al.*, 1997) in view of Granoff *et al.* (*J. Pediatr.* 121: 187-194, 1992), Vella *et al.* (*Biotechnology* 20: 1-22, 1992) and Frasch (*In: Development and Clinical Uses of Haemophilus B conjugate Vaccines.* (Ed) Willis *et al.* M. Dekker, New York, pages 435-453, 1994).

The transition limitation 'comprising' similar to 'having', 'including', 'containing', or 'characterized by', represent open-ended claim language and therefore, do not exclude additional, unrecited elements. See MPEP 2111.03 [R-1]. See *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986)*; *In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ('comprising' leaves 'the claim open for the inclusion of unspecified ingredients even in major amounts').

Granoff *et al.* (1997) taught an immunogenic combination vaccine composition comprising immunologically effective amounts of group C *Neisseria meningitidis* oligosaccharide-CRM197 conjugate, a *Haemophilus influenzae* b oligosaccharide-CRM197 conjugate, and the generally well tolerated MF59 adjuvant. See 'Materials and Methods'; Results; Figure 1; and page 1710. Granoff

et al. reported on the most important finding on the augmented or enhanced serum antibody response to both anti-group C *Neisseria meningitidis* and anti-*Haemophilus influenzae* b induced by the MF59 adjuvant. See left column on page 1714.

Granoff *et al*. (1997) do not teach the presence of the proteosomic vesicles such as outer membrane vesicles from serogroup B *Neisseria meningitidis* in their immunogenic vaccine composition.

However, Granoff *et al*. (1992) taught an immunogenic PRP-OMP conjugate comprising *Haemophilus influenzae* type b (Hib) polysaccharide conjugated to *Neisseria meningitidis* outer membrane protein complex (i.e., OMVs) which was more immunogenic than a conjugate comprising Hib oligomers conjugated to CRM197 after one or two doses. Granoff's (1992) conjugate comprising *Haemophilus influenzae* type b (Hib) polysaccharide conjugated to *Neisseria meningitidis* OMP complex elicited earlier acquisition of serum antibody than the conjugate comprising Hib oligomers conjugated to CRM197 in infants in three geographic regions. See abstract. Granoff's (1992) conjugate comprising *Haemophilus influenzae* type b (Hib) polysaccharide conjugated to *Neisseria meningitidis* outer membrane protein complex (i.e., OMVs) elicited significant increases in serum antibody levels after a single injection at 2 months of age whereas the HbOC conjugate vaccine required additional doses at 4 and 6 months of age to elicit a comparable antibody response. Granoff *et al*. (1992) expressly taught that the OMP carrier has been reported to have adjuvant properties for both T cell-dependent and T cell-independent antigens and has also been reported to be mitogenic unlike the CRM carrier protein used in HbOC conjugate vaccine. See the paragraph bridging pages 191 and 192. That the PRP-OMP or PRP-OMPC conjugate, is known by the commercial name PedvaxHIB, and that it comprises Hib capsular oligosaccharides conjugated to the outer membrane protein complex or OMPC (i.e., OMVs) obtained from serogroup B *Neisseria meningitidis* by deoxycholate extraction process is implied in the prior art teachings in light of what is known in the art. For example, Vella *et al*. taught that the PRP-OMPC conjugate is known by its commercial name, PedvaxHIB, and that it comprises OMVs from serogroup B *Neisseria meningitidis* obtained by deoxycholate extraction process. See the last paragraph on page 3; and Table 1-1. Liekwise, Table 1 and section V on page 444 of the Frasch reference taught that the FDA-approved Merck Hib PRP-OMPC vaccine, also known as PRP-OMP or PedvaxHIB, comprises size-reduced polysaccharide (i.e., oligosaccharide) of Hib conjugated to

meningococcal outer membrane *vesicles*. Frasch further characterized the Hib PRP-OMPC vaccine as having a number of *unique* properties such as induction of a strong immune response in infants after the first dose, and the OMV protein carrier not being a component of the DTP vaccine. See section V of Frasch.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace the *Haemophilus influenzae* b oligosaccharide-CRM197 conjugate in Granoff's (1997) immunogenic combination vaccine composition with Granoff's ('1992) more immunogenic PRP-OMP conjugate comprising *Haemophilus influenzae* type b (Hib) oligosaccharide conjugated to *Neisseria meningitidis* OMVs, which was known in the art to elicit earlier acquisition of serum antibody than a conjugate comprising Hib oligomers conjugated to CRM197 as taught by . Granoff *et al.* (1992) to produce the immunogenic composition of the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a combination conjugate vaccine that includes a Hib conjugate that is more immunogenic than a conjugate comprising Hib oligomers conjugated to CRM197 after one or two doses and that advantageously elicits earlier acquisition of serum antibody than the conjugate comprising Hib oligomers conjugated to CRM197 in infants in three geographic regions Granoff *et al.* (1992), or that has a number of *unique* properties such as induction of a strong immune response in infants after the first dose, and the OMV protein carrier not being a component of the DTP vaccine as taught by Frasch.

Claims 17-19, 22 and 25 are *prima facie* obvious over the prior art of record.

13) Claim 21 is rejected under 35 U.S.C § 103(a) as being unpatentable over Granoff *et al.* (*Infect. Immun.* 65: 1710-1715, May 1997, of record) (Granoff *et al.*, 1997) as modified by Granoff *et al.* (*J. Pediatr.* 121: 187-194, 1992), Vella *et al.* (*Biotechnology* 20: 1-22, 1992) and Frasch (*In*: *Development and Clinical Uses of Haemophilus B conjugate Vaccines.* (Ed) Willis *et al.* M. Dekker, New York, pages 435-453, 1994) as applied to claim 17 above, and further in view of Dalseg *et al.* (*In*: *Vaccines* 96. (Ed) Brown F. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., pages 177-182, 1996, of record).

The teachings of Granoff *et al.* (1997) as modified by Granoff *et al.* (1992), Vella *et al.* and Frasch are explained above, which are silent on the serogroup B *Neisseria meningitidis* strain being strain 44/76.

However, the use of serogroup B *Neisseria meningitidis* strain H44/76 for obtaining OMVs for use in a vaccine was well known in the art at the time of the invention. For instance, Dalseg *et al.* had demonstrated that an OMV preparation obtained from *N. meningitidis* strain 44/76 (B:15:P1.7, 16:L3,7,9) served as a protective vaccine in humans. See page 177.

Given Dalseg's express teaching that meningococcal OMVs from *N. meningitidis* strain 44/76 (B:15:P1.7, 16:L3,7,9) served as a protective vaccine in humans, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use Dalseg's *N. meningitidis* strain 44/76 (B:15:P1.7, 16:L3,7,9) to make OMVs in Granoff's (1997) immunogenic composition as modified by Granoff *et al.* (1992), Vella *et al.* and Frasch to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing in Granoff's (1997) immunogenic composition as modified by Granoff *et al.* (1992), Vella *et al.* and Frasch OMVs from the serogroup B meningococcal strain 44/76 that was already demonstrated in the art to serve as a protective vaccine in humans as taught by Dalseg *et al.*

Claim 21 is *prima facie* obvious over the prior art of record.

14) Claim 24 is rejected under 35 U.S.C § 103(a) as being unpatentable over Granoff *et al.* (*Infect. Immun.* 65: 1710-1715, May 1997, of record) (Granoff *et al.*, 1997) as modified by Granoff *et al.* (*J. Pediatr.* 121: 187-194, 1992), Vella *et al.* (*Biotechnology* 20: 1-22, 1992) Frasch (*In*: *Development and Clinical Uses of Haemophilus B conjugate Vaccines.* (Ed) Willis *et al.* M. Dekker, New York, pages 435-453, 1994) as applied to claim 17 above, and further in view of Seid (US 6,638,513, of record) ('513) or Granoff (WO 98/58670) ('670).

The reference of Seid ('513) is used in this rejection because it qualifies as prior art under 35 U.S.C § 102(e) and therefore is not disqualified as prior art under 35 U.S.C § 103(a).

The teachings of Granoff *et al.* (1997) as modified by Granoff *et al.* (1992), Vella *et al.* and Frasch are explained above, which do not teach their composition to be further comprising polylactic acids or polyglycolic acids.

However, the use of polylactic acids or polyglycolic acids in combination with a meningococcal oligosaccharide conjugate was well known in the art at the time of the instant invention. For instance, Seid ('513) taught combining carriers, such as, polylactic or polyglycolic acids with meningococcal glycoconjugates for the purpose of primary vaccination wherein the

carriers do not themselves induce the production of harmful antibodies. See lines 10-18 in column 9. Similarly, Granoff ('670) taught the routine use of polylactic acids and/or polyglycolic acids in combination with a meningococcal oligosaccharide conjugate. Granoff ('670) taught combining carriers, such as, polylactic and polyglycolic acids with meningococcal glycoconjugates for the purpose of primary vaccination wherein the carriers do not themselves induce the production of harmful antibodies. See lines 27-33 on page 11.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Seid's ('513) or Granoff's ('670) polylactic or polyglycolic acids to Granoff's (1997) immunogenic composition as modified by Granoff *et al.* (1992), Vella *et al.* and Frasch to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Granoff's (1997) immunogenic composition as modified by Granoff *et al.* (1992), Vella *et al.* and Frasch for primary vaccination without inducing the production of harmful antibodies as taught by Seid ('513) or Granoff ('670).

Claim 24 is *prima facie* obvious over the prior art of record.

Remarks

15) Claims 17-19, 21, 22, 24, 25 and 28 stand rejected.

Claim 20 is objected to as being dependent from a rejected claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 26, 27 and 30 are allowable.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

17) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

18) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

April, 2009